



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant : WATSON et al.  
Appl. No. : 09/975,317  
Filed : October 12, 2001  
Title : METHOD

Confirmation No: 8178

TC/A.U. : 1618  
Examiner : M. HARTLEY

Docket No.: : WATS3001C/REF  
Customer No: : 23364

**APPEAL BRIEF 37 CFR §41.37**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

This brief on appeal is submitted along with the required fee of \$500.00 under § 41.20(b)(2) for a large entity. The period for filing the brief has been extended to expire on October 22, 2005, by the filing herewith of a Petition for a Four Month Extension of Time and payment of the required fee.

Any additional fees necessary for this appeal may be charged against the undersigned's Deposit Account No. 02-0200.

**41.37 (c)(1)(i). REAL PARTY IN INTEREST**

The real party in interest is Amersham Health AS.

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41.37 (c)(1)(ii). RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences with respect to the claimed invention which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal known to appellants, appellants' legal representative or assignee.

41.37 (c)(1)(iii). STATUS OF CLAIMS

This application contains 96 claims. Claims 1-75, 82, 83, 87, 94, and 95 have been canceled from the application without prejudice or disclaimer. Appellants reserve the right to file a further continuation application to any subject matter described and /or claimed in the application as originally filed which is not the subject of this appeal.

Claims 76-81, 84-86, 88-93 and 96 are pending in the application and have been finally rejected. Claims 76-81, 84-86, 88-93 and 96 are the claims on appeal.

41.37 (c)(1)(iv). STATUS OF AMENDMENTS

An amendment was filed after the Final Rejection and the amendment entered subject to filing a notice of appeal as stated in the Advisory Action mailed September 20, 2005. The required notice of appeal has been filed. The claims remaining in the application are claims 76-81, 84-86, 88-93 and 96. These are the claims on appeal.

41.37 (c)(1)(v). SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to improvements in and relating to magnetic resonance imaging, in particular to a method of MR imaging enabling early detection of myocardial ischemia. (Page 1, lines 1-4.)

It has now surprisingly been found that the cellular process of manganese uptake is greatly retarded during early ischemia thereby providing for the possibility of using manganese contrast agents in a method of functional myocardial imaging. (Page 3, lines 30-35.)

It has now surprisingly been found that substantially lower, clinically acceptable, dosages of manganese may be used in fast or ultra-fast imaging techniques to provide an effective method of myocardial imaging, in particular to provide important information about myocardial viability during or following a severe heart attack or coronary occlusion. (Page 3 line 31 to page 4, line 4.)

Preferably, the method of the invention provides a method of functional imaging which may discriminate between normal tissue, reversibly and irreversibly injured tissue during ischemia and during reperfusion. In particular, the invention provides a means for discriminating between reversibly and irreversibly injured tissue. (Page 5, lines 5-11.)

The claimed invention thus provides a method of distinguishing viable myocardial tissue from necrotic (infarcted) tissue, the method comprising administering to a body a physiologically acceptable manganese complex or salt thereof, within a period of from 3 to 6 hours following administration of said complex or salt thereof subjecting said body to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium of said body and distinguishing viable myocardial tissue from infarcted tissue. (Page 9, lines 10-20.)

41.37 (c)(1)(vi). GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The first ground of rejection to be reviewed on appeal is the rejection of claims 75-77, 79-82 and 87-95 as anticipated under 35 U.S.C. 102(b) by the teaching of Rocklage, U.S. Patent 5,190,744.

The second ground of rejection to be reviewed on appeal is the rejection of claims 83-86 under 35 U.S.C. 103 as being prima facie obvious over Rocklage, U.S. Patent 5,190,744 in view of Rocklage, U. S. Patent 4,889,931.

The third and final ground of rejection to be reviewed on appeal is the rejection of claim 78, as being prima facie obvious under 35 U.S.C. 103 over Rocklage, U.S. Patent 5,190,744 in view of Goldenberg, U. S. Patent 5,632,968.

41.37 (c)(1)(vii). ARGUMENT

I. THE ANTICIPATION REJECTION

The amendment filed after Final Rejection adds new independent claim 96 to the application. Claim 96 is the only independent claim in the application and is a combination of the subject matter from canceled claims 75, 82 and 83. Claim 83 is not included in the anticipation rejection as set forth in the Final Rejection. Therefore, the anticipation rejection set forth in the Final Rejection has been obviated since new independent claim 96 contains the limitation from canceled claim 83 which was not included in the anticipation rejection.

In this regard, Appellants wish to direct the Examiner's attention to MPEP § 2131 which states that to anticipate a claim, the reference must teach every element of the claim.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed.Cir. 1990).

Accordingly, since the limitation from claim 83 is included in claim 96, it is most respectfully requested that the rejection on the grounds of anticipation under 35 U.S.C. 102(b) with respect to the Rocklage U.S. Patent 5,190,744 be withdrawn or reversed on appeal.

It is believed that the Examiner has tacitly agreed that the anticipation rejection is no longer maintained in view of the lack of comments in the Advisory Action which appear to be restricted to the obviousness rejection.

## II. THE OBVIOUSNESS REJECTIONS

### The legal standard

With respect to an obviousness rejection, Appellants wish to direct the Examiner's attention to the basic requirements of a prima facie case of obviousness as set forth in the MPEP § 2143. This section states that to establish a prima facie case of obviousness, three basic criteria first must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Section 2143.03 states that all claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Appellants also most respectfully direct the Examiner's attention to MPEP § 2144.08 (page 2100-114) wherein it is stated that Office personnel should consider all rebuttal argument and evidence presented by applicant and the citation of In re Soni for error in not considering evidence presented in the specification.

A. Claims 83-86 are not prima facie obvious under 35 USC 103(a) over Rocklage U.S. Patent 5,190,744 in view of Rocklage U. S. Patent 4,889,931

It is urged in the Advisory Action that the amendment after final does not place the application in condition for allowance because: the combination of references teaches all of the steps as claimed, i.e., using known MRI contrast agent in known methods of MRI imaging of infarcted heart tissue. The asserted difference of distinguishing is urged to be accomplished by analyzing a series of images taken, which is disclosed by the prior art. The practitioner would have been motivated to interpret the results by looking at the images in the same manner as claimed. The act of examining the images obtained appears to be the difference in the claimed method, e.g., distinguishing between tissues. This analysis is said not to be seen as a patentable difference, as only thinking steps are involved. In reference to the argument between the coronary and myocardial tissue, it is noted that myocardial tissue is usually used to define the heart as a whole including the coronary arteries. Note, Rocklage discloses

imaging infarcted tissue as claimed in the preamble. Appellants most respectfully traversed these conclusions and statements.

Appellants wish to point out that the method claimed in claim 96 (claim 96 includes the limitations from claim 83 which has been canceled from the application) has a number of specific limitations as would be appreciated by one of ordinary skill in the art to which the invention pertains, which cannot be ignored and must be considered in evaluating the patentability of the claimed subject matter. These limitations are neither taught nor suggested by the prior art relied upon in the rejection.

Claim 96 claims a method of distinguishing viable myocardial tissue from necrotic (infarcted) tissue in a human or nonhuman body. The claims on appeal relate to the detection of myocardial ischemia whereas Rocklage '744 is concerned with the detection of cerebral (brain) ischemia as is evident from the detailed discussion and working examples contained in the patent. Although Rocklage '744 also teaches that the same method would be useful in the detection of coronary ischemia, the myocardium and coronary arteries are different parts of the heart - the myocardium is the middle muscular layer of the heart wall, and coronary arteries surround the heart and branch out from the aorta to supply blood to the heart as would be appreciated by one of ordinary skill in the art. There is no motivation in Rocklage '744 to the claimed invention and obvious to try is not the standard of obviousness under 35 USC 103. Moreover, the only suggestion of distinguishing myocardial tissue is in Appellants' specification which may not be used as a teaching reference. In *re Fritch*, 23 USPQ 1780, 1784 (Fed Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps."). Rocklage '744 does not therefore describe a method of detecting myocardial ischemia as in the presently claimed invention.

Moreover, the specific method claimed in claim 96 can be further distinguished from the prior art. Rocklage '744 does not disclose a method of distinguishing between reversibly injured tissue and irreversibly injured tissue, a claim limitation which cannot be ignored. Rocklage describes only a method for detecting ischemia. Ischemia is a decrease of blood supply which leads to an inadequate supply of oxygen where the

blood supply is limited as would be appreciated by one of ordinary skill in the art. Again, the necessary motivation to make this determination is not in the prior art but only in Appellants' disclosure which is not available as a teaching reference.

Independent claim 96 is directed to a method of distinguishing viable myocardial tissue from necrotic (infarcted) tissue. Ischemia leads to the damage of tissue to which the patient's blood supply has been affected. The extent of the tissue damage within a patient can vary such that the damage to some tissue is reversible, whereas the damage to other tissue is not. Claim 96 is limited to a method for distinguishing between these types of tissue following/during an ischemic event. Such a method is nowhere disclosed or suggested in Rocklage '744 as would be appreciated by one of ordinary skill in the art.

Claim 96 is limited in administering to the body a physiologically acceptable manganese complex wherein the manganese complex is a manganese chelate complex having a  $K_a$  value of from  $10^7$  to  $10^{25}$  and a formula (I) or a salt thereof as specifically defined in the claim and at a dosage of 0.001 to 0.2 mmol/kg bodyweight. These are claim limitations which cannot be ignored.

The contrast agents described in Rocklage '744, in particular the Dy-compounds described in the Examples of '744, are blood pool agents and are detected in the blood supply by MRI as would be appreciated by one of ordinary skill in the art to which the invention pertains. As a result, the method described in Rocklage '744 can only be used to identify and/or monitor abnormal or modified blood flow. The method does not involve or allow for the detection of damaged tissue in accordance with the claims on appeal. Again, a limitation which cannot be ignored. The method claimed of the claims on appeal relies on the contrast agent used being able to distinguish between reversibly and irreversibly injured myocardial tissue. This is achieved using the contrast agents defined in the claims on appeal. The manganese contrast agents of the claimed invention dissociate once they have been administered into the body and the resulting manganese ions are able to enter viable (i.e. repairable) myocardial cells via  $Ca^{2+}$  channels. It should be noted that one of ordinary skill in the art would appreciate that not all metal ions are capable of being taken up by cells via  $Ca^{2+}$  channels. The manganese ions are not however able to enter myocardial cells which are irreversibly damaged. The



manganese ions generate a signal in MRI imaging, thereby generating a signal in the viable myocardial cells. Since manganese ions cannot be taken up by irreversibly damaged cells, no such signal is generated in necrotic (infarcted) cells.

The method claimed in claim 96 on appeal is therefore able to distinguish between the two types of cells. This is much more than the “thinking” step as referred to in the Advisory action. It is the result of Appellants’ teaching with respect to the specified dissociation constant, as specified in the claims, and the selection of the contrast agent of formula (I) as taught by Appellants and specified in the claims on appeal that the advantageous process of the present invention is obtained.

Appellants acknowledge that Rocklage ‘744 does refer to manganese ions. However, this reference forms part of the general teaching provided by the patent. It is recognized at the top of page 4 of the Official Action of July 16, 2004, incorporated by reference into the Final Rejection, that Rocklage ‘744 teaches that various known chelating agents may be employed in column 4, but fails to specifically disclose the use of the same contrast agents as instantly claimed (e.g., manganese complexes, such as, those of formula I (claim 55) [now claim 96] and dosages thereof. The preference for the contrast agents is the lanthanide ion, especially high spin lanthanides such as ions of Dy, Dd, Eu and Ho, in particular Dy(III). This leads one of ordinary skill in the art, away from the contrast agents used in the presently claimed invention. It is acknowledged that Rocklage ‘744 mentions Mn as one of several possible metals but there is nothing to lead to this particular metal in place of Dy as the clear preference.

The Final Rejection attempts to overcome these deficiencies in Rocklage ‘744 by relying on the teachings of the reference to manganese chelates in Rocklage ‘931. This represents no more than an obvious to try standard of obviousness since Rocklage ‘744 does not disclose a method for distinguishing between reversibly and irreversibly injured myocardial tissue as discussed above and nor does Rocklage ‘931.

The level of one of ordinary skill in the art must be taken into consideration as well as the teachings of the reference as a whole. It should be noted that Dy-contrast agents are particularly preferred as noted at column 4 lines 1-7 of the ‘744 reference. This is a teaching away from the manganese contrast agents of the presently claimed invention.

Only Dy-contrast agents are employed in the Examples of Rocklage '744, and Dy-contrast agents are not suitable for detecting the viability of myocardial cells. This is because Dy-contrast agents are taken up neither by viable myocardial cells nor by irreversibly damaged myocardial cells. Consequently, a method employing such contrast agents is not able to distinguish between the two types of cells in accordance with the presently claimed invention.

Moreover, Dy is the chemical symbol for Dysprosium which is an element of the lanthanide series and not a transition metal such as manganese used in the method of the present invention. Mn is included in the list of at column 4 but this requires a selection and again requires the improper application of the obvious to try standard. Appellants note the Examiner's reference to claim 26 but this includes the limitation from claim 1 and there is no support for the limited grouping identified in the claim in the specification.

Claim 96 also requires that within a period of from 3 to 6 hours following administration of the Mn complex or salt to the body, the body is subjected to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium of said body and distinguishing viable myocardial tissue from infarcted tissue; with the proviso that said manganese complex or salt thereof is the only contrast agent administered in the method. There is no discussion in the Final Rejection of where in the references relied upon in the rejection is the teaching for these additional limitations.

The method as claimed in claim 96 can therefore be distinguished from the methods described in the prior art. Furthermore, it is submitted that the claimed method is not obvious since a method for distinguishing reparable myocardial cells from irreparable cells is nowhere disclosed in the prior art. None of the prior art documents even address the problem of distinguishing reparable cells from irreparable cells. Furthermore, neither is there anything in the prior art to suggest that manganese contrast agents would dissociate when administered to a patient, nor that the resulting manganese ions would be taken up by viable myocardial tissue and not by necrotic tissue. The skilled person would not therefore be led to the claimed method from the

cited prior art. Common knowledge and common sense of person of ordinary skill in the art is no good to reject under 35 USC 103(a); In re Lee 61 USPQ2d 1430 (CAFC 2002), teachings in the prior art are required. Accordingly, it is most respectfully requested that this rejection be withdrawn or reversed on appeal.

B. Claim 78 is not prima facie obvious under 35 USC 103(a) over Rocklage U.S. Patent 5,190,744 in view of Goldenberg U. S. Patent 5,632,968

It is urged in the Final Rejection that Rocklage '744 teaches that "various varieties of echo planar imaging (EPI) are particularly suitable" in column 2, lines 20-23, but fails to specifically disclose that the echo imaging is an inversion recovery echo imaging method. It is then urged that Godenberg discloses methods of imaging cardiovascular lesions and teaches that inversion recovery is a well know and equivalent method of spin-echo MRI, with reference to column 13, lines 23-48 of the patent. It is concluded that it would be obvious to one of ordinary skill in the art to further modify the methods disclosed by Rocklage to use inversion-recovery spin-echo MRI as the spin echo MRI procedure because it is well known in the art that this is a useful and equivalent method of spin-echo MRI as taught by Goldenberg. Appellants' make no admission with respect to the correctness of the Examiner's comments as stated in this rejection. It is most respectfully submitted that the claim 78 is dependent on claim 77 which is dependent on claim 96, the sole independent claim on appeal.

As previously noted, claim 96 is limited administering to the body a physiologically acceptable manganese complex wherein the manganese complex is a manganese chelate complex having a  $K_a$  value of from  $10^7$  to  $10^{25}$  and a formula (I) or a salt thereof as specifically defined in the claim and at a dosage of 0.001 to 0.2 mmol/kg bodyweight. These are claim limitations which cannot be ignored.

The contrast agents described in Rocklage '744, in particular the Dy-compounds described in the Examples of '744, are blood pool agents and are detected in the blood supply by MRI as would be appreciated by one of ordinary skill in the art to which the

invention pertains. As a result, the method described in Rocklage '744 can only be used to identify and/or monitor abnormal or modified blood flow. The method does not involve or allow for the detection of damaged tissue in accordance with the claims on appeal.

The method claimed of the claims on appeal relies on the contrast agent used being able to distinguish between reversibly and irreversibly injured myocardial tissue. This is achieved using the contrast agents defined in the claims on appeal. The manganese contrast agents of the claimed invention dissociate once they have been administered into the body and the resulting manganese ions are able to enter viable (i.e. repairable) myocardial cells via  $\text{Ca}^{2+}$  channels. It should be noted that one of ordinary skill in the art would appreciate that not all metal ions are capable of being taken up by cells via  $\text{Ca}^{2+}$  channels. The manganese ions are not however able to enter myocardial cells which are irreversibly damaged. The manganese ions generate a signal in MRI imaging, thereby generating a signal in the viable myocardial cells. Since manganese ions cannot be taken up by irreversibly damaged cells, no such signal is generated in necrotic (infarcted) cells.

The method claimed in present claim 96 is therefore able to distinguish between the two types of cells. This is much more than the "thinking" step as referred to in the Advisory action. It is the result of Appellants' teaching with respect to the specified dissociation constant as specified in the claims and the selection of the agent of formula (I) as taught by Appellants' and specified in the claims on appeal.

Appellants acknowledge that Rocklage '744 does refer to manganese ions. However, this reference forms part of the general teaching provided by the document. It is recognized at the top of page 4 of the Official Action of July 16, 2004, incorporated by reference into the Final Rejection, that Rocklage '744 teaches that various known chelating agents may be employed in column, but fails to specifically disclose the use of the same contrast agents as instantly claimed (e.g., manganese complexes, such as, those of formula I (claim 55) [now claim 96] and dosages thereof.

The Final Rejection attempts to overcome these deficiencies in Rocklage '744 by relying on the teachings of the reference to manganese chelates in Rocklage '931. This reference is not applied in the present rejection but even if it were, this represents no

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more than an obvious to try standard of obviousness since Rocklage '744 does not disclose a method for distinguishing between reversibly and irreversibly injured myocardial tissue as discussed above and nor does Rocklage '931. Accordingly, this rejection should also be withdrawn or reversed on appeal.

## CONCLUSION

In view of the above arguments, the rejections of the claims on appeal should not be sustained on appeal. The rejections should be reversed and the application passed to issue.

Respectfully submitted,

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41.37 (c)(1)(viii) Claims appendix

76. A method as claimed in claim 96 wherein said magnetic resonance imaging procedure is one capable of generating images with time intervals of less than 100 milliseconds.

77. A method as claimed in claim 96 wherein said imaging procedure is a gradient echo or echo planar imaging procedure.

78. A method as claimed in claim 77 wherein said imaging procedure is an inversion recovery echo planar imaging procedure.

79. A method as claimed in claim 77 wherein said imaging procedure is one in which TI (inversion time) is 100 to 800 msec.

80. A method as claimed in claim 96 wherein said manganese complex or salt thereof is administered at a dosage of 0.005 to 0.2 mmol/kg bodyweight.

81. A method as claimed in claim 80 wherein said manganese complex or salt thereof is administered at a dosage of 0.01 to 0.05 mmol/kg bodyweight.

84. A method as claimed in claim 96 wherein in formula I:  
R<sup>5</sup> is hydroxy, C<sub>1-8</sub> alkoxy, ethylene glycol, glycerol, amino or C<sub>1-8</sub> alkylamido;  
X is a bond or a group selected from CH<sub>2</sub>, (CH<sub>2</sub>)<sub>2</sub>, CO, CH<sub>2</sub>CO, CH<sub>2</sub>CH<sub>2</sub>CO or CH<sub>2</sub>COCH<sub>2</sub>;  
Y is a bond;  
R<sup>6</sup> is a mono- or poly(hydroxy or alkoxy) alkyl group or a group of the formula OP(O)(OR<sup>8</sup>)R<sup>7</sup>; and  
R<sup>7</sup> is hydroxy or an unsubstituted alkyl or aminoalkyl group.

85. A method as claimed in claim 96 wherein in formula I,  $R^3$  is ethylene and each group  $R^1$  represents  $-CH_2COR^5$  in which  $R^5$  is hydroxy.

86. A method as claimed in claim 96 in which the compound of formula I is N,N'-bis-(pyridoxal-5-phosphate)-ethylenediamine-N,N'-diacetic acid (DPDP) or N,N'-dipyridoxyl-ethylenediamine-N,N'-diacetic acid (PLED).

88. A method as claimed in claim 96 wherein said magnetic resonance imaging procedure is carried out within a period of up to 6 hours after the administration of said complex or salt thereof to said body.

89. A method as claimed in claim 96 wherein the contrast medium further comprises calcium chelate complexes.

90. A method as claimed in claim 96 wherein the contrast medium further comprises calcium or sodium salts.

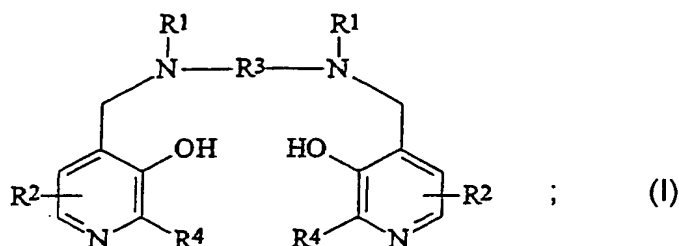
91. A method as claimed in claim 90 wherein the calcium salt comprises calcium chloride, calcium ascorbate, calcium gluconate or calcium lactate.

92. A method as claimed in claim 96 wherein the contrast medium further comprises physiologically compatible buffers.

93. A method as claimed in claim 96 wherein the contrast medium further comprises an antioxidant such as ascorbic acid or a reducing sugar.

96. A method of distinguishing viable myocardial tissue from necrotic (infarcted) tissue in a human or nonhuman body, said method comprising administering to said body a physiologically acceptable manganese complex wherein said manganese complex is a manganese chelate complex having a  $K_a$  value of from  $10^7$  to  $10^{25}$  and a

formula I:



or a salt thereof

(wherein in formula I

each R<sup>1</sup> independently represents hydrogen or -CH<sub>2</sub>COR<sup>5</sup>;

R<sup>5</sup> represents hydroxy, optionally hydroxylated alkoxy, amino or alkylamido;

each R<sup>2</sup> independently represents a group XYR<sup>6</sup>;

X represents a bond, or a C<sub>1-3</sub> alkylene or oxoalkylene group optionally substituted by a group R<sup>7</sup>;

Y represents a bond, an oxygen atom or a group NR<sup>6</sup>;

R<sup>6</sup> is a hydrogen atom, a group COOR<sup>8</sup>, an alkyl, alkenyl, cycloalkyl, aryl or aralkyl group optionally substituted by one or more groups selected from COOR<sup>8</sup>, CONR<sup>8</sup><sub>2</sub>, NR<sup>8</sup><sub>2</sub>, OR<sup>8</sup>, =NR<sup>8</sup>, =O, OP(O)(OR<sup>8</sup>)R<sup>7</sup> and OSO<sub>3</sub>M;

R<sup>7</sup> is hydroxy, an optionally hydroxylated, optionally alkoxylated alkyl or aminoalkyl group;

R<sup>8</sup> is a hydrogen atom or an optionally hydroxylated, optionally alkoxylated alkyl group;

M is a hydrogen atom or one equivalent of a physiologically tolerable cation;

R<sup>3</sup> represents a C<sub>1-8</sub> alkylene group, a 1,2-cycloalkylene group, or a 1,2-arylene group; and

each R<sup>4</sup> independently represents hydrogen or C<sub>1-3</sub> alkyl);

at a dosage of 0.001 to 0.2 mmol/kg bodyweight, within a period of from 3 to 6 hours following administration of said complex or salt thereof subjecting said body to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium



of said body and distinguishing viable myocardial tissue from infarcted tissue; with the proviso that said manganese complex or salt thereof is the only contrast agent administered in said method.

(ix) Evidence appendix

NONE

(X) Related proceedings appendix

NONE